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TITLE: Antisense modulation of cot oncogene expression

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The cot enzyme is localized to the cytoplasm and exists in two different forms, a long form and a truncated or short form, which are products of alternative initiation mechanisms. These two forms have differing transforming activities and it is rearrangement of the C-terminus that increases cellular transformation (Aoki et al., *Oncogene*, 1991, 6, 1515-1519; Aoki et al., *J. Biol. Chem.*, 1993, 268, 22723-22732). Expression of cot oncogene is increased

upon treatment of cells with interleukin-1, a cytokine involved in inflammation or okadaic acid, a well-known tumor promoter (Chan et al., *Oncogene*, 1993, 8, 1329-1333). In the rat, it has been demonstrated that the cot oncogene is involved in mouse mammary tumor virus (MMTV) associated transformation of mammary gland cells (Erny et al., *Oncogene*, 1996, 13, 2015-2020). The pharmacological modulation of cot oncogene activity and/or expression may therefore be an appropriate point of therapeutic intervention in pathological conditions such as inflammation, cancer and disorders of the immune system.